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Docket No: C38435/109700CON

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of :

Akira ASAKURA *et al.*

Serial No.: 09/470,667

Filed: December 22, 1999

For: **NOVEL ALCOHOL/ALDEHYDE DEHYDROGENASES**

Examiner: M. Walicka

Art Unit: 1652

Commissioner for Patents
Washington, DC 20231

SECOND DECLARATION OF DR. MASAKO SHINJOH UNDER 37 C.F.R. § 1.132

Sir:

I, Masako Shinjoh, a citizen and resident of Japan, hereby declare as follows:

1. I am employed by Nippon Roche Research Center of Nippon Roche K.K., Kajiwara 200, Kamakura-shi, Kanagawa-ken 247-8530, Japan (hereafter "NRKK"). I currently hold the position of genetic engineer at NRKK. A copy of my *curriculum vitae* is attached as Exhibit 1.

2. I am a coinventor of U.S. patent application No: 09/470,667 (the '667 application). The '667 application is summarized in more detail in the FIRST DECLARATION OF DR. MASAKO SHINJOH UNDER 37 C.F.R. § 1.132 ("First Declaration") filed concurrently herewith.

3. As described in the First Declaration, after reviewing the Sequence Listing filed with the '667 application, how the nucleotide and amino acid sequences that make up the Sequence Listing were incorporated into the '667 application, and the original nucleotide printouts from the sequencing machine used to read the experimentally derived sequences, I have come to the conclusion that SEQ ID NOs:1, 3, and 7 each contain a single base (SEQ ID NOs:1 and 3) or a single amino acid (SEQ ID NO:7) error that arose through typing errors.

4. After the '667 application was filed, I found discrepancies in the nucleotide and amino acid sequences identified in the '667 application as SEQ ID NO: 1, SEQ ID NO: 3, and SEQ ID NO: 7, respectively when compared to the computer printouts generated by the nucleotide sequencing machine used to read the nucleotide sequences that ultimately became SEQ ID NOs:1 and 3 in the '667 application. As set forth in more detail below, I believe that each of these discrepancies was the result of a typing mistake made when I prepared the sequence listing data for an internal Research Report.

5. The original sequence data underlying each of the sequences disclosed in the Sequence Listing of the '667 application were generated by a nucleotide sequencing machine, and could not be converted into an electronic file for manipulation in an electronic

medium (*e.g.*, a word processor). Accordingly, I manually typed the sequences ultimately disclosed in the '667 application into an electronic format using the original sequence data generated by the nucleotide sequencing machine. It is my belief that when the original sequence data was retyped into an electronic format that a single base in each of SEQ ID NOs:1 and 3 was entered in error, and that because of the error in SEQ ID NO:3, its deduced amino acid sequence (SEQ ID NO:7) also contained a single amino acid error. The manually re-typed sequences, including the unrecognized typographical mistakes, were then incorporated into the foreign priority application (EP 96115001 filed September 19, 1996), which became the basis for the '667 application including the Sequence Listing contained therein. (Exhibit 2).

6. A copy of the original printout from the nucleotide sequencing machine of the open reading frame of Enzyme A including the nucleotide sequence (which became SEQ ID NO:1 in the '667 application) and its deduced amino acid sequence (which became SEQ ID NO:5 in the '667 application) is attached as Exhibit 3. I have compared the nucleotide and deduced amino acid sequences from the original printout with the sequences disclosed as SEQ ID NOs:1 and 5 in the '667 application, and have found that the nucleotide at position 852 of SEQ ID NO:1 is a "G" whereas the corresponding nucleotide in the original printout is a "C." It is my

belief that the correct nucleotide at position 852 is "C," not "G" as recited in SEQ ID NO:1.

7. Because of the redundancy of the genetic code, when SEQ ID NO:1 was translated, the deduced amino acid encoded by the codon containing the nucleotide at position 852 did not change compared to the deduced amino acid sequence generated by the nucleotide sequencer as set forth in the original printout. Thus, both sequences are identical.

8. A copy of the original printout from the nucleotide sequencing machine of the open reading frame of Enzyme A" including the nucleotide sequence (which became SEQ ID NO:3 in the '667 application) and its deduced amino acid sequence (which became SEQ ID NO:7 in the '667 application) is attached as Exhibit 4. I have compared the nucleotide and deduced amino acid sequences from the original printout with the sequences disclosed as SEQ ID NOs:3 and 7 in the '667 application and have found that the nucleotide at position 644 of SEQ ID NO:3 is an "A" whereas the corresponding nucleotide in the original printout is a "C." It is my belief that the correct nucleotide at position 644 is "C," not "A" as recited in SEQ ID NO:3.

9. The replacement of "A" for "C" at position 644 in SEQ ID NO:3 also led to the translation of a different amino acid ("Asn" was translated

instead of "Thr" at position 192) from the codon containing the error at nucleotide position 644. It is my belief that the correct amino acid at position 192 of SEQ ID NO:7 is "Thr," not "Asn" as currently recited.

10. To verify the correctness of the nucleotide and amino acid sequences identified on the original printouts generated by the nucleotide sequencing machine, which were the bases for the disclosure of SEQ ID NOs:1, 3, and 7 in the '667 application, I obtained a sample of *Gluconobacter oxydans* strain DSM 4025, the same microorganism from which the nucleotide sequences of SEQ ID NOs:1 and 3 were isolated (as disclosed in the '667 application), from the International Depository Authority, Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH ("DSMZ"), a publicly available cell depository.

11. With the assistance of Mr. Naoki Itoh, NRKK's Patent & Licensing Manager, I then contracted with an independent nucleotide sequencing company (Sawady – see the First Declaration) to use the *Gluconobacter oxydans* DSM 4025 cell sample I obtained from DSMZ to clone and sequence the relevant parts of the chromosomal DNA of these cells.

12. The chain of custody of the cell sample and chromosomal DNA derived therefrom is set forth in my First Declaration and the

DECLARATION OF MR. MASAO MASHITA UNDER 37 C.F.R. § 132 and of the DECLARATION OF MR. YOSHITAKA MURATA UNDER 37 C.F.R. §1.132, both of which are being filed concurrently herewith.

13. With respect to the sequence work, I instructed Sawady to utilize two primer pairs designed by the coinventors for the cloning (by polymerase chain reaction (PCR)) and sequencing of Enzyme A (Primers for Analysis 1) and of Enzyme A" (Primers for Analysis 2) as described below.

Primers for Analysis 1: (for Enzyme A)
Forward: A697f 5'- TACGAAGCCC GTTGGATGAC -3'
Reverse: A1000r 5'- TCGGGTTGAT CGACTGCAGA -3'

Primers for Analysis 2: (for Enzyme A")
Forward: A"479f 5'- TATTCGACGT CGATCGCGGT -3'
Reverse: A"780r 5'- AACTGCTGAG GTGCCGTAGT -3'

14. The Primers for Analysis 1 were designed to amplify (by PCR) the region from nucleotide (nt) position 697 to nt position 1000 of the gene encoding Enzyme A and to determine the amplified nucleotide sequence having 304 bases including the nucleotide at position 852. The primers for Analysis 2 were designed to amplify (by PCR) the region from nt position 479 to nt position 780 of the gene encoding Enzyme A" and to determine the amplified nucleotide sequence having 302 bases including the nucleotide at position 644.

15. The primer information was provided to Mr. Masao Mashita at

Sawady together with a sample of the original microorganism DSM 4025 disclosed in the '667 application (and obtained through DSMZ) to facilitate the cloning and sequencing of the relevant nucleotides for Enzyme A (SEQ ID NO:1) and Enzyme A" (SEQ ID NO:3). (*See* my First Declaration).

16. On October 13, 2000, I received from Sawady, via Mr. Itoh, an Experimental Report (non-finalized) including the sequence data, which are set forth in Exhibit 5. From the anti-parallel alignment of the (+) and (–) strands in combination with the sequence information of the primers used, I confirmed the correctness of the two nucleotide sequences set forth below. For determining each sequence, I took into consideration that at positions downstream of each primer used in the PCR sequencing carried out by Sawady, the nucleotide reading on the sense strand was not absolutely reliable, and thus for each such region, the data from the complementary sequence was used:

Ex. (1): A697-1000 Sawady [304 bp] (corresponds to Enzyme A, *i.e.* SEQ ID NO: 1)

```
697
 TACGAAGCCC GTTGGATGAC CGGTGCCTGG GGCCAGATCA CCTATGACCC

 CGTCACCAAC CTTGTCCACT ACGGCTCGAC CGCTGTGGGT CCGGCGTCGG

 AAACCCAACG CGGCACCCCG GGCGGCACGC TGTACGGCAC GAACACCCGT
    852
 TTCGCCGTGC GTCCTGACAC GGGCGAGATT GTCTGGCGTC ACCAGACCCT

 GCCCCGCGAC AACTGGGACC AGGAATGCAC GTTCGAGATG ATGGTCACCA

 ATGTGGATGT CCAACCCTCG ACCGAGATGG AAGGTCTGCA GTCGATCAAC
```

1000
CCGA

17. The correctness of the above-identified sequence was verified with the two nucleotide sequences (41F903 and 39F903) (Exhibit 5) and two primer sequences (A697f and A1000r):

* Nucleotides 697-716 of Ex(1) above are the same as nucleotides 1-20 of primer A697f;
* Nucleotides 717-966 of Ex(1) above are the same as nucleotides 41-290 of the complementary sequence of 41F903;
* Nucleotides 967-980 of Ex(1) above are the same as nucleotides 253-266 of 39F903; and
* Nucleotides 981-1000 of Ex(1) above are the same as nucleotides 1-20 of the complementary sequence of primer A1000r.

Ex. (2): A"479-780 Sawady [302 bp] (corresponds to Enzyme A", *i.e.* SEQ ID NO: 3)

479
TATTCGACGT CGATCGCGGT CAAGGCACGG ATATGGTCTC GAACTCGTCC

GGCCCGATTG TCGCCAATGG CGTCATCGTT GCGGGCTCGA CCTGTCAGTA

TTCGCCGTTC GGCTGTTTCG TTTCGGGCCA CGACTCGGCC ACCGGTGAAG
644
AGCTGTGGCG CAACACCTTT ATCCCGCGCG CCGGCGAAGA GGGTGATGAG

ACCTGGGGCA ATGATTACGA GGCCCGCTGG ATGACCGGCG TTTGGGGCCA

GATCACCTAT GACCCCGTTG GCGGCCTTGT CCACTACGGC ACCTCAGCAG
780
TT

18. The correctness of the above-identified sequence was verified with two nucleotide sequences (45F903 and 43F903) (Exhibit 5) and two primer sequences (A"479f and A"780r):

* Nucleotides 479-498 of Ex(2) above are the same as nucleotides 1-20 of primer A"479f;
* Nucleotides 499-728 of Ex(2) above are the same as nucleotides 41-270 of the complementary sequence of 45F903;
* Nucleotides 729-760 of Ex(2) above are the same as nucleotides 228-259 of 43F903; and
* Nucleotides 761-780 of Ex(2) above are the same as nucleotides 1-20 of the complementary sequence of primer A"780r.

19. Based on my knowledge and experience, and in view of the results presented herein, it is my opinion that SEQ ID NOs:1 and 3 of the '667 application each contain a single nucleotide error introduced by a typing mistake. The single mistake in SEQ ID NO:1 resulted in no error in the amino acid sequence of SEQ ID NO: 5. The single mistake in SEQ ID NO: 3 when translated resulted in a single amino acid error in SEQ ID NO: 7. Each of these errors is readily identifiable to one of skill in the art by cloning and sequencing the chromosomal DNA of the same microorganism used in the '667 application, which is publicly available. The identification of each of these errors is summarized in more detail below:

(a) SEQ ID NO: 1

By comparing the nucleotide sequence identified above as "A697-1000 Sawady [304 bp]" with the nucleotide sequence recited in the original nucleotide printout from the nucleotide sequencing machine (Exhibit 3), I confirmed that the nucleotides from positions 697-1000 in each sequence are identical. Therefore, the nucleotide at position 852 in SEQ ID NO: 1 ("G") is incorrect and should read "C." This error had no effect on the corresponding deduced amino acid sequence in SEQ ID NO:5.

(b) SEQ ID NO: 3

By comparing the nucleotide sequence identified above as "A"479-780 Sawady [302 bp]" with the nucleotide sequence recited in the original nucleotide printout from the nucleotide sequencing machine (Exhibit 4), I confirmed that the nucleotides from positions 479-780 in each sequence are identical. Therefore, the nucleotide at position 644 in SEQ ID NO: 3 ("A") is incorrect and should read "C."

(c) SEQ ID NO:7

Based on the correct nucleotide sequence for SEQ ID NO: 3, the triplet codon recited as "AAC" of nucleotide positions 643-645 in SEQ ID NO:3 should read "ACC." This should be reflected in the corresponding deduced amino acid sequence (SEQ ID NO: 7) at amino acid position 192, which was recited as "Asn" in the current

Sequence Listing. The correct codon ("ACC"), however, corresponds to the amino acid "Thr." Therefore, the amino acid at position 192 in SEQ ID NO:7 ("Asn") is incorrect and should read "Thr."

20. In sum, on the basis of the data presented herein, resequencing of the relevant parts of the chromosomal DNA of a sample of the same microorganism from which SEQ ID NOs:1 and 3 were isolated as disclosed in the '667 application (*i.e.*, *Gluconobacter oxydans* strain DSM 4025) confirms that typographical mistakes resulted in the following errors found in SEQ ID NOs: 1, 3, and 7, and that such errors would be readily identified by one skilled in this art using publicly available starting materials and routine skill. Accordingly, in my opinion, one skilled in this art would recognize, after resequencing the relevant parts of the chromosomal DNA of DSM 4025 that:

(1) The nucleotide at position 852 of SEQ ID NO:1, which currently recites "G," should recite "C."

(2) The nucleotide at position 644 of SEQ ID NO:3, which currently recites "A," should recite "C."

(3) The amino acid at position 192 of SEQ ID NO:7, which currently recites "Asn," should recite "Thr."

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: September 18, 2002

Masako Shinjoh

Masako Shinjoh

CURRICULUM VITAE of Masako Shinjoh As of August 28, 2002

Scientist
Department of Applied Microbiology
Nippon Roche K.K.
Nippon Roche Research Center
200 Kajiwara Kamakura, Japan
247-8530.

Phone: +81-467-47-2226
FAX: +81-467-45-6812
E-mail: masako.shinjoh@roche.com

Education & Research Experience:

1a. Scientist (April 1979 to date) at Dept of Applied Microbiology, Nippon Roche K.K., Nippon Roche Research Center at Kamakura, Japan, which belongs to Vitamin and Fine Chemical Division in Hoffmann-La Roche

This work includes improvement of microorganisms producing vitamin or its precursor by conventional method and genetic engineering.

1b. Visiting scientist (Jan. to March 1982) at Research Institute of Molecular Biology at Nutley, NJ, USA, which belonged to Hoffmann-La Roche. Objectives: to exchange scientific information and technical transfer of genetic engineering skills.

2. Ph.D. (Jan. 12, 1996)
Ph.D. in Engineering from Department of Fermentation Technology, Osaka University, Osaka, Japan.

The title of the Thesis is "Metabolic engineering for 2-keto-L-gulonic acid production in

Gluconobacter".

3. Master Degree (April 1977 to March 1979)

Master in Engineering from Department of Fermentation Technology, Osaka University, Osaka, Japan.

The projects involved were

"Characterization of bacteriophage of bacitracin-produing *Bacillus*"

"Application of plasmid on fermentation production: factors responsible for stabilization of hybrid plasmids carrying trytophane operon in *E. coli* ."

4. Bachelar Degree (April 1975 to March 1977)

Department of Fermentation Technology, Osaka University, Osaka, Japan.

The projects involved were

"In vitro synthesis of alpha-amylase of *Bacillus*"

5. Professional field

Microbiology
Fermentation technology
Genetic engineering

6. Memberships

a) The Society for Bioscience and Bioengineering
b) Japan Society for Bioscience, Biotechnology, and Agrochemistry

7. Personal information:

Female,
Japanese citizen,
Birthday: 20th February, 1955

LIST OF PUBLICATIONS

Original Papers by the Author

Shinjoh, M., Y. Setoguchi, T. Hoshino and A. Fujiwara. (1990)
L-Sorbose dissimilation in 2-keto-L-gulonic acid-producing mutant UV10 derived from *Gluconobacter melanogenus* IFO 3293. Agric. Biol. Chem. 54: 2257 - 2263.

Shinjoh, M., T. Sugisawa, S. Masuda, and T. Hoshino. (1994)
Efficient conversion of L-sorbosone to 2-keto-L-gulonic acid by *Acetobacter liquefaciens* strains. J. Ferment. Bioeng. 78: 476 - 478.

Shinjoh, M., and T. Hoshino. (1995). Development of a stable shuttle vector and a conjugative transfer system for *Gluconobacter oxydans*.J. Ferment. Bioeng. 79: 95 - 99.

Shinjoh, M., N. Tomiyama, A. Asakura, and T. Hoshino. (1995) Cloning and nucleotide sequencing of membrane-bound L-sorbosone dehydrogenase gene of *Acetobacter liquefaciens* IFO 12258 and its expression in *Gluconobacter oxydans*. Appl. Environ. Microbiol. 43: 1064 - 1069.

Shinjoh, M, M., Tazoe, and T. Hoshino. (2002) NADPH-dependent L-sorbose reductase is responsible for L-sorbose assimilation in *Gluconobacter suboxydans* IFO 3291. J. of Bacteriol., 84: 861 - 863.

Miyazaki, T., N. Tomiyama, M. Shinjoh, and T. Hoshino. (2002) Molecular cloning and functional expression of D-sorbitol dehydrogenase from *Gluconobacter suboxydans* IFO3255 which requires PQQ and hydrophobic protein SldB for the activity development in *E.coli*. (2001) Biosci. Biotechnol. Biochem. 66: 262-270. (the corresponding author)

Shinjoh, M., N. Tomiyama, T. Miyazaki, and T. Hoshino. (2002) Main polyol dehydrogenase of *Gluconobacter suboxydans* IFO 3255, membrane-bound D-sorbitol dehydrogenase, that needs product of upstream gene, *sldB*, for activity. Biosci. Biotechnol. Biochem. (in press)

Other Publications on the work done at Hoffmann-La Roche

Sugisawa, T., T. Hoshino, S. Masuda, S. Nomura, Y. Setoguchi, M. Tazoe, M. Shinjoh, S. Someha and A. Fujiwara. (1990) Microbial production of 2-keto-L-gulonic acid from L-sorbose and D-sorbitol by *Gluconobacter oxydans*. Agric. Biol. Chem. 54: 1201 - 1209.

Hoshino, T., T. Sugisawa, M. Tazoe, M. Shinjoh and A. Fujiwara. (1990) Metabolic pathway for 2-keto-L-gulonic acid formation in *Gluconobacter oxydans* IFO 3293. Agric. Biol. Chem. 54: 1211 - 1218.

Shinjoh, M., (1990) Biotechnology of acetic acid bacteria. Su no kagaku, Asakura shoten. Tokyo. 157 - 170. (in Japanese)

Other Publications on the work done at Osaka Univ.

Imanaka, T., K. Uchida, M. Tateishi (Shinjoh), and S. Aiba. (1979) Inducible bacteriophage of *Bacillus licheniformis* ATCC 10716. Virology 95: 249 - 250.

Tsunekawa, H., M. Tateishi (Shinjoh), T. Imanaka, S. Aiba. (1981) TnA-directed deletion of the trp operon from RSF2124-trp in *Escherichia coli*.

Patent publication: USP granted including "M. Shinjoh" as the inventor

(as of Aug. 28, 2002)

	PAT. NO.	Title
1	6,407,203	Cytochrome *c* and polynucleotides encoding cytochrome *c*
2	6,146,860	Manufacture of L-ascorbic acid and D-erythorbic acid
3	6,127,156	D-sorbitol dehydrogenase gene
4	6,037,147	Cytochrome *c* and polynucleotides encoding cytochrome *c*
5	5,541,108	*Gluconobacter oxydans* strains

6 5,399,496 DNA shuttle vectors for *E. coli*, *Gluconobacter*, and *Acetobacter*

7 5,352,599 Co-enzyme-independent L-sorbosone dehydrogenase of *Gluconobacter oxydans*: isolation, characterization, and cloning and autologus expression of the gene

----------END of CV----------

2nd Masaki Shinjoh Declaration Exhibit - 2

SEQUENCE LISTING

(1) GENERAL INFORMATION

(i) APPLICANT

NAME: F. HOFFMANN-LA ROCHE AG

STREET: Grezacherstrasse 124

CITY: Basle

COUNTRY: Switzerland

POSTAL CODE: CH-4002

TELEPHONE: 061 - 688 25 11

FAX: 061 - 688 13 95

TELEX: 962292/965542 hlr c

(ii) TITLE OF INVENTION:

Alcohol/Aldehyde dehydrogenase genes

(iii) NUMBER OF SEQUENCES: 8

(iv) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk

(B) COMPUTER: Macintosh

(C) OPERATING SYSTEM:

(D) SOFTWARE: MS word ver 5.1

(v) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER:

(B) FILING DATE:

(C) CLASSIFICATION

CCAAGGCGAA GACATGGTTT CGAACTCGTC GGGCCCGATC GTGGCAAACG 550

GCGTGATCGT TGCCGGTTCG ACCTGCCAAT ACTCGCCGTT CGGCTGCTTT 600

GTCTCGGGCC ACGACTCGGC CACCGGTGAA GAGCTGTGGC GCAACTACTT 650

CATCCCGCGC GCTGGCGAAG AGGGTGATGA GACTTGGGGC AACGATTACG 700

AAGCCCGTTG GATGACCGGT GCCTGGGGCC AGATCACCTA TGACCCCGTC 750

ACCAACCTTG TCCACTACGG CTCGACCGCT GTGGGTCCGG CGTCGGAAAC 800

CCAACGCGGC ACCCCGGGCG GCACGCTGTA CGGCACGAAC ACCCGTTTCG 850

CGGTGCGTCC TGACACGGGC GAGATTGTCT GGCGTCACCA GACCCTGCCC 900

CGCGACAACT GGGACCAGGA ATGCACGTTC GAGATGATGG TCACCAATGT 950

GGATGTCCAA CCCTCGACCG AGATGGAAGG TCTGCAGTCG ATCAACCCGA 1000

ACGCCGCAAC TGGCGAGCGT CGCGTGCTGA CCGGCGTTCC GTGCAAAACC 1050

GGCACCATGT GGCAGTTCGA CGCCGAAACC GGCGAATTCC TGTGGGCCCG 1100

TGATACCAAC TACCAGAACA TGATCGAATC CATCGACGAA AACGGCATCG 1150

TGACCGTGAA CGAAGATGCG ATCCTGAAGG AACTGGATGT TGAATATGAC 1200

GTCTGCCCGA CCTTCTTGGG CGGCCGCGAC TGGCCGTCGG CCGCACTGAA 1250

CCCCGACAGC GGCATCTACT TCATCCCGCT GAACAACGTC TGCTATGACA 1300

TGATGGCCGT CGATCAGGAA TTCACCTCGA TGGACGTCTA TAACACCAGC 1350

AACGTGACCA AGCTGCCGCC CGGCAAGGAT ATGATCGGTC GTATTGACGC 1400

GATCGACATC AGCACGGGTC GTACGCTGTG GTCGGTCGAA CGTGCTGCGG 1450

CGAACTATTC GCCCGTCTTG TCGACCGGCG GCGGCGTTCT GTTCAACGGT 1500

GGTACGGATC GTTACTTCCG CGCCCTCAGC CAAGAAACCG GCGAGACCCT 1550

GTGGCAGACC CGCCTTGCAA CCGTCGCGTC GGGCCAGGCC ATCTCTTACG 1600

AGGTTGACGG CATGCAATAT GTCGCCATCG CAGGTGGTGG TGTCAGCTAT 1650

GGCTCGGGCC TGAACTCGGC ACTGGCTGGC GAGCGAGTCG ACTCGACCGC 1700

CATCGGTAAC GCCGTCTACG TCTTCGCCCT GCCGCAATAA 1740

INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1740 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) ORIGINAL SOURCE:

ORGANISM: *Gluconobacter oxydans*

STRAIN: DSM 4025

(iv) FEATURE:

FEATURED KEY: CDS

POSITIOIN: 1..1737

SEQUENCING METHOD: E

```
ATGAAGACGT CGTCTTTGCT GGTTGCGAGC GTTGCCGCGC TTGCAAGCTA   50
TAGCTCCTTT GCGCTTGCTC AAGTGACCCC CGTCACCGAT GAATTGCTGG  100
CGAACCCGCC CGCTGGTGAA TGGATCAGCT ACGGTCAGAA CCAAGAAAAC  150
TACCGTCACT CGCCCCTGAC GCAGATCACG ACTGAGAACG TCGGCCAACT  200
GCAACTGGTC TGGGCGCGCG GCATGCAGCC GGGCAAAGTC CAAGTCACGC  250
CCCTGATCCA TGACGGCGTC ATGTATCTGG CAAACCCGGG CGACGTGATC  300
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CAGGCCATCG ACGCCAAAAC TGGCGATCTG ATCTGGGAAC ACCGCCGCCA 350

ACTGCCGAAC ATCGCCACGC TGAACAGCTT TGGCGAGCCG ACCCGCGGCA 400

TGGCGCTGTA CGGCACCAAC GTTTACTTTG TTTCGTGGGA CAACCACCTG 450

GTCGCCCTCG ACACCGCAAC TGGCCAAGTG ACGTTCGACG TCGACCGCGG 500

CCAAGGCGAA GACATGGTTT CGAACTCGTC GGGCCCGATC GTGGCAAACG 550

GCGTGATCGT TGCCGGTTCG ACCTGCCAAT ACTCGCCGTT CGGCTGCTTT 600

GTCTCGGGCC ACGACTCGGC CACCGGTGAA GAGCTGTGGC GCAACTACTT 650

CATCCCGCGC GCTGGCGAAG AGGGTGATGA GACTTGGGGC AACGATTACG 700

AAGCCCGTTG GATGACCGGC GTCTGGGGTC AGATCACCTA TGACCCCGTT 750

GGCGGCCTTG TCCACTACGG CTCGTCGGCT GTTGGCCCGG CTTCGGAAAC 800

CCAGCGCGGC ACCACCGGCG GCACCATGTA CGGCACCAAC ACCCGTTTCG 850

CTGTCCGTCC CGAGACTGGC GAGATCGTCT GGCGTCACCA AACTCTGCCC 900

CGCGACAACT GGGACCAAGA GTGCACCTTC GAGATGATGG TTGCCAACGT 950

TGACGTGCAG CCCGCAGCTG ACATGGACGG CGTCCGCTCG ATCAACCCGA 1000

ACGCCGCCAC CGGCGAGCGT CGCGTTCTGA CCGGCGTTCC GTGCAAAACC 1050

GGCACCATGT GGCAGTTCGA CGCCGAAACC GGCGAATTCC TGTGGGCCCG 1100

TGACACCAGC TACGAGAACA TCATCGAATC GATCGACGAA AACGGCATCG 1150

TGACCGTCGA CGAGTCGAAA GTTCTGACCG AGCTGGACAC CCCCTATGAC 1200

GTCTGCCCGC TGCTGCTGGG TGGCCGTGAC TGGCCGTCGG CTGCGCTGAA 1250

CCCCGATACC GGCATCTACT TTATCCCGCT GAACAACACC TGCATGGATA 1300

TCGAAGCTGT CGACCAGGAA TTCAGCTCGC TGGACGTGTA CAACCAAAGC 1350

CTGACCGCCA AAATGGCACC GGGTAAAGAG CTGGTTGGCC GTATCGACGC 1400

CATCGACATC AGCACAGGCC GCACCCTGTG GACCGCTGAG CGCGAAGCCT 1450

CGAACTACGC GCCTGTCCTG TCGACCGCTG GCGGCGTTCT GTTCAACGGC 1500

GGCACCGACC GTTACTTCCG CGCTCTCAGC CAAGAGACCG GCGAGACCCT 1550

GTGGCAGACC CGTCTGGCGA CTGTCGCTTC GGGCCAAGCT GTCTCGTACG 1600

AGATCGACGG CGTCCAATAC ATCGCCATCG GCGGCGGCGG CACGACCTAT 1650

GGTTCGTTCC ACAACCGTCC CCTGGCCGAG CCGGTCGACT CGACCGCGAT 1700

CGGTAATGCG ATGTACGTCT TCGCGCTGCC CCAGCAATAA 1740

INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1737 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) ORIGINAL SOURCE:

ORGANISM: *Gluconobacter oxydans*

STRAIN: DSM 4025

(iv) FEATURE:

FEATURE KEY: CDS

POSITIOIN: 1..1734

SEQUENCING METHOD: E

ATGAAACTGA CGACCCTGCT GCAAAGCAGC GCCGCCCTGC TTGTGCTTGG 50

CACCATTCCC GCCCTTGCCC AAACCGCCAT CACCGATGAA ATGCTGGCGA 100

ACCCGCCCGC TGGTGAATGG ATCAACTACG GTCAGAACCA AGAGAACTAC 150

CGCCACTCGC CCCTGACGCA GATTACCGCA GACAACGTCG GCCAACTGCA 200

ACTGGTCTGG GCGCGCGGTA TGGAAGCGGG CAAGATCCAA GTGACCCCGC 250

TTGTCCATGA CGGCGTCATG TATCTGGCAA ACCCCGGTGA CGTGATCCAG 300

GCCATCGACG CCGCGACCGG CGATCTGATC TGGGAACACC GCCGCCAACT 350

GCCGAACATC GCCACGCTGA ACAGCTTTGG TGAGCCGACC CGCGGCATGG 400

CCCTCTATGG CACCAACGTC TATTTCGTCT CGTGGGACAA CCACTTGGTC 450

GCGCTGGACA CCTCGACCGG CCAAGTCGTA TTCGACGTCG ATCGCGGTCA 500

AGGCACGGAT ATGGTCTCGA ACTCGTCCGG CCCGATTGTC GCCAATGGCG 550

TCATCGTTGC GGGCTCGACC TGTCAGTATT CGCCGTTCGG CTGTTTCGTT 600

TCGGGCCACG ACTCGGCCAC CGGTGAAGAG CTGTGGCGCA ACAACTTTAT 650

CCCGCGCGCC GGCGAAGAGG GTGATGAGAC CTGGGGCAAT GATTACGAGG 700

CCCGCTGGAT GACCGGCGTT TGGGGCCAGA TCACCTATGA CCCCGTTGGC 750

GGCCTTGTCC ACTACGGCAC CTCAGCAGTT GGCCCTGCGG CCGAGATTCA 800

GCGCGGCACC GTTGGCGGCT CGATGTATGG CACCAACACC CGCTTTGCTG 850

TCCGCCCCGA GACCGGCGAG ATCGTCTGGC GTCACCAAAC TCTGCCCCGC 900

GACAACTGGG ACCAAGAGTG TACGTTCGAG ATGATGGTCG TCAACGTCGA 950

CGTCCAGCCC TCGGCTGAGA TGGAAGGCCT GCACGCCATC AACCCCGATG 1000

CCGCCACGGG CGAGCGTCGC GTTGTGACCG GCGTTCCGTG CAAGAACGGC 1050

ACCATGTGGC AGTTCGACGC CGAAACCGGC GAATTCCTGT GGGCGCGCGA 1100

CACCAGCTAT CAGAACCTGA TCGAAAGCGT CGATCCCGAT GGTCTGGTGC 1150

ATGTGAACGA AGATCTGGTC GTGACCGAGC TGGAAGTGGC CTATGAAATC 1200

TGCCCGACCT TCCTGGGTGG CCGCGACTGG CCGTCGGCTG CGCTGAACCC 1250

CGATACTGGC ATCTATTTCA TCCCGCTGAA CAACGCCTGT AGCGGTATGA 1300

CGGCTGTCGA CCAAGAGTTC AGCTCGCTCG ATGTGTATAA CGTCAGCCTC 1350

GACTATAAAC TGTCGCCCGG TTCGGAAAAC ATGGGCCGTA TCGACGCCAT 1400

CGACATCAGC ACCGGCCGCA CGCTGTGGTC GGCTGAACGC TACGCCTCGA 1450

ACTACGCGCC TGTCCTGTCC ACCGGCGGCG GCGTGCTGTT CAACGGCGGC 1500

ACCGACCGTT ACTTCCGCGC CCTCAGCCAA GAGACCGGCG AGACGCTGTG 1550

GCAGACCCGT CTGGCGACTG TCGCCTCGGG TCAAGCGATT TCCTATGAGA 1600

TCGACGGCGT GCAATATGTC GCCATCGGGC GCGGCGGCAC CAGCTATGGC 1650

AGCAACCACA ACCGCGCCCT GACCGAGCGG ATCGACTCGA CCGCCATCGG 1700

CAGCGCGATC TATGTCTTTG CTCTGCCGCA GCAGTAA 1737

INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1740 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) ORIGINAL SOURCE:

ORGANISM: *Gluconobacter oxydans*

STRAIN: DSM 4025

(iv) FEATURE:

FEATURE KEY: CDS

POSITIOIN: 1..1737

SEQUENCING METHOD: E

ATGAACCCCA CAACGCTGCT TCGCACCAGC GCGGCCGTGC TATTGCTTAC 50

CGCGCCCGCC GCATTCGCGC AGGTAACCCC GATTACCGAT GAACTGCTGG 100

CGAACCCGCC CGCTGGTGAA TGGATTAACT ACGGCCGCAA CCAAGAAAAC 150

TATCGCCACT CGCCCCTGAC CCAGATCACT GCCGACAACG TTGGTCAGTT 200

GCAACTGGTC TGGGCCCGCG GGATGGAGGC GGGGGCCGTA CAGGTCACGC 250

CGATGATCCA TGATGGCGTG ATGTATCTGG CAAACCCCGG TGATGTGATC 300

CAGGCGCTGG ATGCGCAAAC AGGCGATCTG ATCTGGGAAC ACCGCCGCCA 350

ACTGCCCGCC GTCGCCACGC TAAACGCCCA AGGCGACCGC AAGCGCGGCG 400

TCGCCCTTTA CGGCACGAGC CTCTATTTCA GCTCATGGGA CAACCATCTG 450

ATCGCGCTGG ATATGGAGAC GGGCCAGGTC GTATTCGATG TCGAACGTGG 500

ATCGGGCGAA GACGGCTTGA CCAGTAACAC CACGGGGCCG ATTGTCGCCA 550

ATGGCGTCAT CGTCGCGGGT TCCACCTGCC AATATTCGCC CTATGGATGC 600

TTTATCTCGG GGCACGATTC CGCGACGGGT GAGGAGCTGT GGCGCAACCA 650

CTTTATCCCG CAGCCGGGCG AAGAGGGTGA CGAGACTTGG GGCAATGATT 700

TCGAGGCGCG CTGGATGACC GGCGTCTGGG GTCAGATCAC CTATGATCCC 750

GTGACGAACC TTGTGTTCTA TGGCTCGACC GGCGTGGGCC CAGCGTCCGA 800

AACCCAGCGC GGCACGCCGG GCGGCACGCT GTATGGCACC AACACCCGCT 850

TTGCGGTGCG TCCCGACACG GGCGAGATTG TCTGGCGTCA CCAGACCCTG 900

CCGCGCGACA ACTGGGACCA AGAATGCACG TTCGAGATGA TGGTCGCCAA 950

CGTCGATGTG CAACCCTCGG CCGAGATGGA GGGTCTGCGC GCCATCAACC 1000

CCAATGCGGC GACGGGCGAG CGCCGTGTGC TGACGGGTGC GCCTTGCAAG 1050

ACCGGCACGA TGTGGTCGTT TGATGCGGCC TCGGGCGAAT TCCTGTGGGC 1100

GCGTGATACC AACTACACCA ATATGATCGC CTCGATCGAC GAGACCGGCC 1150

TTGTGACGGT GAACGAGGAT GCGGTGCTGA AAGAGCTGGA CGTTGAATAT 1200

GACGTCTGCC CGACCTTCCT GGGTGGGCGC GACTGGTCGT CAGCCGCACT 1250

GAACCCGGAC ACCGGCATTT ACTTCTTGCC GCTGAACAAT GCCTGCTACG 1300

ATATTATGGC CGTTGATCAA GAGTTTAGCG CGCTCGACGT CTATAACACC 1350

AGCGCGACCG CAAAACTCGC GCCGGGCTTT GAAAATATGG GCCGCATCGA 1400

CGCGATTGAT ATCAGCACCG GGCGCACCTT GTGGTCGGCG GAGCGCCCTG 1450

CGGCGAACTA CTCGCCCGTT TTGTCGACGG CAGGCGGTGT GGTGTTCAAC 1500

GGCGGGACCG ACCGCTATTT CCGTGCCCTC AGCCAGGAAA CCGGCGAGAC 1550

TTTGTGGCAG GCCCGTCTTG CGACGGTCGC GACGGGGCAG GCGATCAGCT 1600

ACGAGTTGGA CGGCGTGCAA TATATCGCCA TCGGTGCGGG CGGTCTGACC 1650

TATGGCACGC AATTGAACGC GCCGCTGGCC GAGGCAATCG ATTCGACCTC 1700

GGTCGGTAAT GCGATCTATG TCTTTGCACT GCCGCAGTAA 1740

INFORMATION FOR SEQ ID NO:5:

(i) **SEQUENCE CHARACTERISTICS:**

(A) **LENGTH: 579 residues**

(B) **TYPE: amino acid**

(C) **TOPOLOGY: linear**

(ii) **MOLECULE TYPE: protein**

(iii) **ORIGINAL SOURCE:**

ORGANISM: *Gluconobacter oxydans*

STRAIN: DSM 4025

(iv) **FEATURE:**

FEATURE KEY: sig peptide

POSITION: -23..-1

SEQUENCING METHOD: E

FEATURE KEY: mat peptide

POSITION: 1..556

SEQUENCING METHOD: E

```
Met Lys Pro Thr Ser Leu Leu Trp Ala Ser Ala Gly Ala Leu Ala
          -20                 -15                 -10

Leu Leu Ala Ala Pro Ala Phe Ala Gln Val Thr Pro Val Thr Asp
          -5                  1                   5

Glu Leu Leu Ala Asn Pro Pro Ala Gly Glu Trp Ile Ser Tyr Gly
      10                  15                  20

Gln Asn Gln Glu Asn Tyr Arg His Ser Pro Leu Thr Gln Ile Thr
      25                  30                  35

Thr Glu Asn Val Gly Gln Leu Gln Leu Val Trp Ala Arg Gly Met
      40                  45                  50

Gln Pro Gly Lys Val Gln Val Thr Pro Leu Ile His Asp Gly Val
      55                  60                  65

Met Tyr Leu Ala Asn Pro Gly Asp Val Ile Gln Ala Ile Asp Ala
      70                  75                  80

Lys Thr Gly Asp Leu Ile Trp Glu His Arg Arg Gln Leu Pro Asn
      85                  90                  95

Ile Ala Thr Leu Asn Ser Phe Gly Glu Pro Thr Arg Gly Met Ala
     100                 105                 110

Leu Tyr Gly Thr Asn Val Tyr Phe Val Ser Trp Asp Asn His Leu
     115                 120                 125

Val Ala Leu Asp Thr Ala Thr Gly Gln Val Thr Phe Asp Val Asp
     130                 135                 140
```

Arg Gly Gln Gly Glu Asp Met Val Ser Asn Ser Ser Gly Pro Ile
145 150 155

Val Ala Asn Gly Val Ile Val Ala Gly Ser Thr Cys Gln Tyr Ser
160 165 170

Pro Phe Gly Cys Phe Val Ser Gly His Asp Ser Ala Thr Gly Glu
175 180 185

Glu Leu Trp Arg Asn Tyr Phe Ile Pro Arg Ala Gly Glu Glu Gly
190 195 200

Asp Glu Thr Trp Gly Asn Asp Tyr Glu Ala Arg Trp Met Thr Gly
205 210 215

Ala Trp Gly Gln Ile Thr Tyr Asp Pro Val Thr Asn Leu Val His
220 225 230

Tyr Gly Ser Thr Ala Val Gly Pro Ala Ser Glu Thr Gln Arg Gly
235 240 245

Thr Pro Gly Gly Thr Leu Tyr Gly Thr Asn Thr Arg Phe Ala Val
250 255 260

Arg Pro Asp Thr Gly Glu Ile Val Trp Arg His Gln Thr Leu Pro
265 270 275

Arg Asp Asn Trp Asp Gln Glu Cys Thr Phe Glu Met Met Val Thr
280 285 290

Asn Val Asp Val Gln Pro Ser Thr Glu Met Glu Gly Leu Gln Ser
295 300 305

Ile Asn Pro Asn Ala Ala Thr Gly Glu Arg Arg Val Leu Thr Gly
310 315 320

Val Pro Cys Lys Thr Gly Thr Met Trp Gln Phe Asp Ala Glu Thr
325 330 335

Gly Glu Phe Leu Trp Ala Arg Asp Thr Asn Tyr Gln Asn Met Ile
340 345 350

Glu Ser Ile Asp Glu Asn Gly Ile Val Thr Val Asn Glu Asp Ala
355 360 365

Ile Leu Lys Glu Leu Asp Val Glu Tyr Asp Val Cys Pro Thr Phe
370 375 380

Leu Gly Gly Arg Asp Trp Pro Ser Ala Ala Leu Asn Pro Asp Ser

385 390 395

Gly Ile Tyr Phe Ile Pro Leu Asn Asn Val Cys Tyr Asp Met Met
400 405 410

Ala Val Asp Gln Glu Phe Thr Ser Met Asp Val Tyr Asn Thr Ser
415 420 425

Asn Val Thr Lys Leu Pro Pro Gly Lys Asp Met Ile Gly Arg Ile
430 435 440

Asp Ala Ile Asp Ile Ser Thr Gly Arg Thr Leu Trp Ser Val Glu
445 450 455

Arg Ala Ala Ala Asn Tyr Ser Pro Val Leu Ser Thr Gly Gly Gly
460 465 470

Val Leu Phe Asn Gly Gly Thr Asp Arg Tyr Phe Arg Ala Leu Ser
475 480 485

Gln Glu Thr Gly Glu Thr Leu Trp Gln Thr Arg Leu Ala Thr Val
490 495 500

Ala Ser Gly Gln Ala Ile Ser Tyr Glu Val Asp Gly Met Gln Tyr
505 510 515

Val Ala Ile Ala Gly Gly Gly Val Ser Tyr Gly Ser Gly Leu Asn
520 525 530

Ser Ala Leu Ala Gly Glu Arg Val Asp Ser Thr Ala Ile Gly Asn
535 540 545

Ala Val Tyr Val Phe Ala Leu Pro Gln
550 555

INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 579 residues

(B) **TYPE:** amino acid

(C) **TOPOLOGY:** linear

(ii) **MOLECULE TYPE:** protein

(iii) **ORIGINAL SOURCE:**

ORGANISM: *Gluconobacter oxydans*

STRAIN: DSM 4025

(iv) **FEATURE:**

FEATURE KEY: sig peptide

POSITION: -23..-1

SEQUENCING METHOD: S

FEATURE KEY: mat peptide

POSITION: 1..556

SEQUENCING METHOD: S

```
Met Lys Thr Ser Ser Leu Leu Val Ala Ser Val Ala Ala Leu Ala
          -20                 -15                 -10

Ser Tyr Ser Ser Phe Ala Leu Ala Gln Val Thr Pro Val Thr Asp
          -5                  1                   5

Glu Leu Leu Ala Asn Pro Pro Ala Gly Glu Trp Ile Ser Tyr Gly
        10                  15                  20

Gln Asn Gln Glu Asn Tyr Arg His Ser Pro Leu Thr Gln Ile Thr
        25                  30                  35

Thr Glu Asn Val Gly Gln Leu Gln Leu Val Trp Ala Arg Gly Met
        40                  45                  50

Gln Pro Gly Lys Val Gln Val Thr Pro Leu Ile His Asp Gly Val
        55                  60                  65
```

Met Tyr Leu Ala Asn Pro Gly Asp Val Ile Gln Ala Ile Asp Ala
70 75 80

Lys Thr Gly Asp Leu Ile Trp Glu His Arg Arg Gln Leu Pro Asn
85 90 95

Ile Ala Thr Leu Asn Ser Phe Gly Glu Pro Thr Arg Gly Met Ala
100 105 110

Leu Tyr Gly Thr Asn Val Tyr Phe Val Ser Trp Asp Asn His Leu
115 120 125

Val Ala Leu Asp Thr Ala Thr Gly Gln Val Thr Phe Asp Val Asp
130 135 140

Arg Gly Gln Gly Glu Asp Met Val Ser Asn Ser Ser Gly Pro Ile
145 150 155

Val Ala Asn Gly Val Ile Val Ala Gly Ser Thr Cys Gln Tyr Ser
160 165 170

Pro Phe Gly Cys Phe Val Ser Gly His Asp Ser Ala Thr Gly Glu
175 180 185

Glu Leu Trp Arg Asn Tyr Phe Ile Pro Arg Ala Gly Glu Glu Gly
190 195 200

Asp Glu Thr Trp Gly Asn Asp Tyr Glu Ala Arg Trp Met Thr Gly
205 210 215

Val Trp Gly Gln Ile Thr Tyr Asp Pro Val Gly Gly Leu Val His
220 225 230

Tyr Gly Ser Ser Ala Val Gly Pro Ala Ser Glu Thr Gln Arg Gly
235 240 245

Thr Thr Gly Gly Thr Met Tyr Gly Thr Asn Thr Arg Phe Ala Val
250 255 260

Arg Pro Glu Thr Gly Glu Ile Val Trp Arg His Gln Thr Leu Pro
265 270 275

Arg Asp Asn Trp Asp Gln Glu Cys Thr Phe Glu Met Met Val Ala
280 285 290

Asn Val Asp Val Gln Pro Ala Ala Asp Met Asp Gly Val Arg Ser
295 300 305

Ile Asn Pro Asn Ala Ala Thr Gly Glu Arg Arg Val Leu Thr Gly

310 315 320

Val Pro Cys Lys Thr Gly Thr Met Trp Gln Phe Asp Ala Glu Thr
325 330 335

Gly Glu Phe Leu Trp Ala Arg Asp Thr Ser Tyr Glu Asn Ile Ile
340 345 350

Glu Ser Ile Asp Glu Asn Gly Ile Val Thr Val Asp Glu Ser Lys
355 360 365

Val Leu Thr Glu Leu Asp Thr Pro Tyr Asp Val Cys Pro Leu Leu
370 375 380

Leu Gly Gly Arg Asp Trp Pro Ser Ala Ala Leu Asn Pro Asp Thr
385 390 395

Gly Ile Tyr Phe Ile Pro Leu Asn Asn Thr Cys Met Asp Ile Glu
400 405 410

Ala Val Asp Gln Glu Phe Ser Ser Leu Asp Val Tyr Asn Gln Ser
415 420 425

Leu Thr Ala Lys Met Ala Pro Gly Lys Glu Leu Val Gly Arg Ile
430 435 440

Asp Ala Ile Asp Ile Ser Thr Gly Arg Thr Leu Trp Thr Ala Glu
445 450 455

Arg Glu Ala Ser Asn Tyr Ala Pro Val Leu Ser Thr Ala Gly Gly
460 465 470

Val Leu Phe Asn Gly Gly Thr Asp Arg Tyr Phe Arg Ala Leu Ser
475 480 485

Gln Glu Thr Gly Glu Thr Leu Trp Gln Thr Arg Leu Ala Thr Val
490 495 500

Ala Ser Gly Gln Ala Val Ser Tyr Glu Ile Asp Gly Val Gln Tyr
505 510 515

Ile Ala Ile Gly Gly Gly Gly Thr Thr Tyr Gly Ser Phe His Asn
520 525 530

Arg Pro Leu Ala Glu Pro Val Asp Ser Thr Ala Ile Gly Asn Ala
535 540 545

Met Tyr Val Phe Ala Leu Pro Gln Gln
550 555

INFORMATION FOR SEQ ID NO:7:

(i) **SEQUENCE CHARACTERISTICS:**

(A) **LENGTH:** 578 residues

(B) **TYPE:** amino acid

(C) **TOPOLOGY:** linear

(ii) **MOLECULE TYPE:** protein

(iii) **ORIGINAL SOURCE:**

ORGANISM: *Gluconobacter oxydans*

STRAIN: DSM 4025

(iv) **FEATURE:**

FEATURE KEY: sig peptide

POSITION: -23..-1

SEQUENCING METHOD: S

FEATURE KEY: mat peptide

POSITION: 1..555

SEQUENCING METHOD: S

```
Met Lys Leu Thr Thr Leu Leu Gln Ser Ser Ala Ala Leu Leu Val
          -20                 -15                 -10

Leu Gly Thr Ile Pro Ala Leu Ala Gln Thr Ala Ile Thr Asp Glu
```

```
-5                  1                   5
Met Leu Ala Asn Pro Pro Ala Gly Glu Trp Ile Asn Tyr Gly Gln
        10                  15                  20
Asn Gln Glu Asn Tyr Arg His Ser Pro Leu Thr Gln Ile Thr Ala
        25                  30                  35
Asp Asn Val Gly Gln Leu Gln Leu Val Trp Ala Arg Gly Met Glu
        40                  45                  50
Ala Gly Lys Ile Gln Val Thr Pro Leu Val His Asp Gly Val Met
        55                  60                  65
Tyr Leu Ala Asn Pro Gly Asp Val Ile Gln Ala Ile Asp Ala Ala
        70                  75                  80
Thr Gly Asp Leu Ile Trp Glu His Arg Arg Gln Leu Pro Asn Ile
        85                  90                  95
Ala Thr Leu Asn Ser Phe Gly Glu Pro Thr Arg Gly Met Ala Leu
       100                 105                 110
Tyr Gly Thr Asn Val Tyr Phe Val Ser Trp Asp Asn His Leu Val
       115                 120                 125
Ala Leu Asp Thr Ser Thr Gly Gln Val Val Phe Asp Val Asp Arg
       130                 135                 140
Gly Gln Gly Thr Asp Met Val Ser Asn Ser Ser Gly Pro Ile Val
       145                 150                 155
Ala Asn Gly Val Ile Val Ala Gly Ser Thr Cys Gln Tyr Ser Pro
       160                 165                 170
Phe Gly Cys Phe Val Ser Gly His Asp Ser Ala Thr Gly Glu Glu
       175                 180                 185
Leu Trp Arg Asn Asn Phe Ile Pro Arg Ala Gly Glu Glu Gly Asp
       190                 195                 200
Glu Thr Trp Gly Asn Asp Tyr Glu Ala Arg Trp Met Thr Gly Val
       205                 210                 215
Trp Gly Gln Ile Thr Tyr Asp Pro Val Gly Gly Leu Val His Tyr
       220                 225                 230
Gly Thr Ser Ala Val Gly Pro Ala Ala Glu Ile Gln Arg Gly Thr
       235                 240                 245
```

Val Gly Gly Ser Met Tyr Gly Thr Asn Thr Arg Phe Ala Val Arg
250 255 260

Pro Glu Thr Gly Glu Ile Val Trp Arg His Gln Thr Leu Pro Arg
265 270 275

Asp Asn Trp Asp Gln Glu Cys Thr Phe Glu Met Met Val Val Asn
280 285 290

Val Asp Val Gln Pro Ser Ala Glu Met Glu Gly Leu His Ala Ile
295 300 305

Asn Pro Asp Ala Ala Thr Gly Glu Arg Arg Val Val Thr Gly Val
310 315 320

Pro Cys Lys Asn Gly Thr Met Trp Gln Phe Asp Ala Glu Thr Gly
325 330 335

Glu Phe Leu Trp Ala Arg Asp Thr Ser Tyr Gln Asn Leu Ile Glu
340 345 350

Ser Val Asp Pro Asp Gly Leu Val His Val Asn Glu Asp Leu Val
355 360 365

Val Thr Glu Leu Glu Val Ala Tyr Glu Ile Cys Pro Thr Phe Leu
370 375 380

Gly Gly Arg Asp Trp Pro Ser Ala Ala Leu Asn Pro Asp Thr Gly
385 390 395

Ile Tyr Phe Ile Pro Leu Asn Asn Ala Cys Ser Gly Met Thr Ala
400 405 410

Val Asp Gln Glu Phe Ser Ser Leu Asp Val Tyr Asn Val Ser Leu
415 420 425

Asp Tyr Lys Leu Ser Pro Gly Ser Glu Asn Met Gly Arg Ile Asp
430 435 440

Ala Ile Asp Ile Ser Thr Gly Arg Thr Leu Trp Ser Ala Glu Arg
445 450 455

Tyr Ala Ser Asn Tyr Ala Pro Val Leu Ser Thr Gly Gly Gly Val
460 465 470

Leu Phe Asn Gly Gly Thr Asp Arg Tyr Phe Arg Ala Leu Ser Gln
475 480 485

Glu Thr Gly Glu Thr Leu Trp Gln Thr Arg Leu Ala Thr Val Ala
490 495 500

```
Ser Gly Gln Ala Ile Ser Tyr Glu Ile Asp Gly Val Gln Tyr Val
      505                 510                 515

Ala Ile Gly Arg Gly Gly Thr Ser Tyr Gly Ser Asn His Asn Arg
      520                 525                 530

Ala Leu Thr Glu Arg Ile Asp Ser Thr Ala Ile Gly Ser Ala Ile
      535                 540                 545

Tyr Val Phe Ala Leu Pro Gln Gln
      550                 555
```

INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 579 residues

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(iii) ORIGINAL SOURCE:

ORGANISM: *Gluconobacter oxydans*

STRAIN: DSM 4025

(iv) FEATURE:

FEATURE KEY: sig peptide

POSITION: -23..-1

SEQUENCING METHOD: E

FEATURE KEY: mat peptide

POSITION: 1..556

SEQUENCING METHOD: E

```
Met Asn Pro Thr Thr Leu Leu Arg Thr Ser Ala Ala Val Leu Leu
-20                 -15                 -10

Leu Thr Ala Pro Ala Ala Phe Ala Gln Val Thr Pro Ile Thr Asp
-5                  1                   5

Glu Leu Leu Ala Asn Pro Pro Ala Gly Glu Trp Ile Asn Tyr Gly
10                  15                  20

Arg Asn Gln Glu Asn Tyr Arg His Ser Pro Leu Thr Gln Ile Thr
25                  30                  35

Ala Asp Asn Val Gly Gln Leu Gln Leu Val Trp Ala Arg Gly Met
40                  45                  50

Glu Ala Gly Ala Val Gln Val Thr Pro Met Ile His Asp Gly Val
55                  60                  65

Met Tyr Leu Ala Asn Pro Gly Asp Val Ile Gln Ala Leu Asp Ala
70                  75                  80

Gln Thr Gly Asp Leu Ile Trp Glu His Arg Arg Gln Leu Pro Ala
85                  90                  95

Val Ala Thr Leu Asn Ala Gln Gly Asp Arg Lys Arg Gly Val Ala
100                 105                 110

Leu Tyr Gly Thr Ser Leu Tyr Phe Ser Ser Trp Asp Asn His Leu
115                 120                 125

Ile Ala Leu Asp Met Glu Thr Gly Gln Val Val Phe Asp Val Glu
130                 135                 140

Arg Gly Ser Gly Glu Asp Gly Leu Thr Ser Asn Thr Thr Gly Pro
145                 150                 155

Ile Val Ala Asn Gly Val Ile Val Ala Gly Ser Thr Cys Gln Tyr
160                 165                 170

Ser Pro Tyr Gly Cys Phe Ile Ser Gly His Asp Ser Ala Thr Gly
```

175 180 185

Glu Glu Leu Trp Arg Asn His Phe Ile Pro Gln Pro Gly Glu Glu
190 195 200

Gly Asp Glu Thr Trp Gly Asn Asp Phe Glu Ala Arg Trp Met Thr
205 210 215

Gly Val Trp Gly Gln Ile Thr Tyr Asp Pro Val Thr Asn Leu Val
220 225 230

Phe Tyr Gly Ser Thr Gly Val Gly Pro Ala Ser Glu Thr Gln Arg
235 240 245

Gly Thr Pro Gly Gly Thr Leu Tyr Gly Thr Asn Thr Arg Phe Ala
250 255 260

Val Arg Pro Asp Thr Gly Glu Ile Val Trp Arg His Gln Thr Leu
265 270 275

Pro Arg Asp Asn Trp Asp Gln Glu Cys Thr Phe Glu Met Met Val
280 285 290

Ala Asn Val Asp Val Gln Pro Ser Ala Glu Met Glu Gly Leu Arg
295 300 305

Ala Ile Asn Pro Asn Ala Ala Thr Gly Glu Arg Arg Val Leu Thr
310 315 320

Gly Ala Pro Cys Lys Thr Gly Thr Met Trp Ser Phe Asp Ala Ala
325 330 335

Ser Gly Glu Phe Leu Trp Ala Arg Asp Thr Asn Tyr Thr Asn Met
340 345 350

Ile Ala Ser Ile Asp Glu Thr Gly Leu Val Thr Val Asn Glu Asp
355 360 365

Ala Val Leu Lys Glu Leu Asp Val Glu Tyr Asp Val Cys Pro Thr
370 375 380

Phe Leu Gly Gly Arg Asp Trp Ser Ser Ala Ala Leu Asn Pro Asp
385 390 395

Thr Gly Ile Tyr Phe Leu Pro Leu Asn Asn Ala Cys Tyr Asp Ile
400 405 410

Met Ala Val Asp Gln Glu Phe Ser Ala Leu Asp Val Tyr Asn Thr
415 420 425

Ser Ala Thr Ala Lys Leu Ala Pro Gly Phe Glu Asn Met Gly Arg
430 435 440

Ile Asp Ala Ile Asp Ile Ser Thr Gly Arg Thr Leu Trp Ser Ala
445 450 455

Glu Arg Pro Ala Ala Asn Tyr Ser Pro Val Leu Ser Thr Ala Gly
460 465 470

Gly Val Val Phe Asn Gly Gly Thr Asp Arg Tyr Phe Arg Ala Leu
475 480 485

Ser Gln Glu Thr Gly Glu Thr Leu Trp Gln Ala Arg Leu Ala Thr
490 495 500

Val Ala Thr Gly Gln Ala Ile Ser Tyr Glu Leu Asp Gly Val Gln
505 510 515

Tyr Ile Ala Ile Gly Ala Gly Gly Leu Thr Tyr Gly Thr Gln Leu
520 525 530

Asn Ala Pro Leu Ala Glu Ala Ile Asp Ser Thr Ser Val Gly Asn
535 540 545

Ala Ile Tyr Val Phe Ala Leu Pro Gln
550 555

INFORMATION FOR SEQ ID NO:9:

(i) **SEQUENCE CHARACTERISTICS:**

(A) **LENGTH:** 82 bases

(B) **TYPE:** nucleotide

(C) **TOPOLOGY:** linear

(ii) **MOLECULE TYPE:** DNA

(iii) **ORIGINAL SOURCE:** synthetic oligonucleotide

CATGAAAATA AAAACAGGTG CACGCATCCT CGCATTATCC GCATTAACGA 50

CGATGATGTT TTCCGCCTCG GCTCTCGCCC AG 82

INFORMATION FOR SEQ ID NO:10:

(i) **SEQUENCE CHARACTERISTICS:**

(A) **LENGTH:** 83 bases

(B) **TYPE:** nucleotide

(C) **TOPOLOGY:** linear

(ii) **MOLECULE TYPE:** DNA

(iii) **ORIGINAL SOURCE:** synthetic oligonucleotide

GTTACCTGGG CGAGAGCCGA GGCGGAAAAC ATCATCGTCG TTAATGCGGA 50

TAATGCGAGG ATGCGTGCAC CTGTTTTTAT TTT 83

INFORMATION FOR SEQ ID NO:11:

(i) **SEQUENCE CHARACTERISTICS:**

(A) **LENGTH:** 27 residues

(B) **TYPE:** amino acid

(C) **TOPOLOGY:** linear

(ii) **MOLECULE TYPE:** peptide

(iii) **ORIGINAL SOURCE:** *E. coli*

(iv) **FEATURE:**

FEATURE KEY: sig peptide

POSITION: 1..26

FEATURE METHOD: S

```
Met Lys Ile Lys Thr Gly Ala Arg Ile Leu Ala Leu Ser Ala Leu
 1               5                  10                  15

Thr Thr Met Met Phe Ser Ala Ser Ala Leu Ala Gln
            20                  25      27
```

INFORMATION FOR SEQ ID NO:12:

(i) **SEQUENCE CHARACTERISTICS:**

(A) **LENGTH:** 27 bases

(B) **TYPE:** nucleotide

(C) **TOPOLOGY:** linear

(ii) **MOLECULE TYPE:** DNA

(iii) **ORIGINAL SOURCE:** synthetic oligonucleotide

GTTAGCGCGG TGGATCCCCA TTGGAGG 27

*** GENIAS - Nucleotide Usage Table ***

DNA Sequence Name (1): pEnzA (1-1740)
Comment :

T	319	(18.3%)
C	559	(32.1%)
A	356	(20.5%)
G	506	(29.1%)
Total	[1740]	

[G+C]% = 61.2 %

*** GENIAS - Codon Usage Table ***
Frame No. 1

DNA Sequence Name (1): pEnzA (1-1740)
Comment :

TTT	Phe	4	0.7%	TCT	Ser	1	0.2%	TAT	Tyr	8	1.4%
TTC	Phe	13	2.2%	TCC	Ser	1	0.2%	TAC	Tyr	14	2.4%
TTA	Leu	0	0.0%	TCA	Ser	0	0.0%	TAA	***	1	0.2%
TTG	Leu	4	0.7%	TCG	Ser	23	4.0%	TAG	***	0	0.0%
CTT	Leu	5	0.9%	CCT	Pro	1	0.2%	CAT	His	1	0.2%
CTC	Leu	2	0.3%	CCC	Pro	11	1.9%	CAC	His	6	1.0%
CTA	Leu	0	0.0%	CCA	Pro	0	0.0%	CAA	Gln	14	2.4%
CTG	Leu	29	5.0%	CCG	Pro	18	3.1%	CAG	Gln	13	2.2%
ATT	Ile	2	0.3%	ACT	Thr	6	1.0%	AAT	Asn	1	0.2%
ATC	Ile	24	4.1%	ACC	Thr	33	5.7%	AAC	Asn	31	5.3%
ATA	Ile	0	0.0%	ACA	Thr	0	0.0%	AAA	Lys	4	0.7%
ATG	Met	16	2.8%	ACG	Thr	12	2.1%	AAG	Lys	3	0.5%
GTT	Val	8	1.4%	GCT	Ala	7	1.2%	GAT	Asp	11	1.9%
GTC	Val	26	4.5%	GCC	Ala	23	4.0%	GAC	Asp	24	4.1%
GTA	Val	0	0.0%	GCA	Ala	11	1.9%	GAA	Glu	21	3.6%
GTG	Val	12	2.1%	GCG	Ala	9	1.6%	GAG	Glu	12	2.1%

TGT	Cys	0	0.0%								
TGC	Cys	6	1.0%								
TGA	***	0	0.0%								
TGG	Trp	16	2.8%								
CGT	Arg	11	1.9%								
CGC	Arg	13	2.2%								
CGA	Arg	1	0.2%								
CGG	Arg	0	0.0%								
AGT	Ser	1	0.2%								
AGC	Ser	7	1.2%								
AGA	Arg	0	0.0%								
AGG	Arg	0	0.0%								
GGT	Gly	16	2.8%								
GGC	Gly	44	7.6%								
GGA	Gly	0	0.0%								
GGG	Gly	0	0.0%								

Total [580]

Dc SM2 EX3 1/2

Nov. 16 '98

A-1

4/1/70

Dc SM2 EX3 2/2

A-2

Ala → Ala
GCC GCG

*** GENIAS - Amino Acid Translation **

DNA Sequence Name (1): pEnzA (1-1740)
Comment :

> Genetic Code [Universal]

```
        10        20        30        40        50        60        70        80        90       100       110       120
ATGAAACCGACTTCGCTGCTTTGGGCCAGTGCTGGCGCACTTGCATTGCTTGCCGCACCCGCCTTTGCTCAAGTGACCCCCGTCACCGATGAATTGCTGGCGAACCCGCCCGCTGGTGAA
 M  K  P  T  S  L  L  W  A  S  A  G  A  L  A  L  L  A  A  P  A  F  A  Q  V  T  P  V  T  D  E  L  L  A  N  P  P  A  G  E

       130       140       150       160       170       180       190       200       210       220       230       240
TGGATCAGCTACGGTCAGAACCAAGAAAACTACCGTCACTCGCCCCTGACGCAGATCACGACTGAGAACGTCGGCCAACTGCAACTGGTCTGGGCGCGCGGCATGCAGCCGGGCAAAGTC
 W  I  S  Y  G  Q  N  Q  E  N  Y  R  H  S  P  L  T  Q  I  T  T  E  N  V  G  Q  L  Q  L  V  W  A  R  G  M  Q  P  G  K  V

       250       260       270       280       290       300       310       320       330       340       350       360
CAAGTCACGCCCCTGATCCATGACGGCGTCATGTATCTGGCAAACCCGGGCGACGTGATCCAGGCCATCGACGCCAAAACTGGCGATCTGATCTGGGAACACCGCCGCCAACTGCCGAAC
 Q  V  T  P  L  I  H  D  G  V  M  Y  L  A  N  P  G  D  V  I  Q  A  I  D  A  K  T  G  D  L  I  W  E  H  R  R  Q  L  P  N

       370       380       390       400       410       420       430       440       450       460       470       480
ATCGCCACGCTGAACAGCTTTGGCGAGCCGACCCGCGGCATGGCGCTGTACGGCACCAACGTTTACTTTGTTTCGTGGGACAACCACCTGGTCGCCCTCGACACCGCAACTGGCCAAGTG
 I  A  T  L  N  S  F  G  E  P  T  R  G  M  A  L  Y  G  T  N  V  Y  F  V  S  W  D  N  H  L  V  A  L  D  T  A  T  G  Q  V

       490       500       510       520       530       540       550       560       570       580       590       600
ACGTTCGACGTCGACCGCGGCCAAGGCGAAGACATGGTTTCGAACTCGTCGGGCCCGATCGTGGCAAACGGCGTGATCGTTGCCGGTTCGACCTGCCAATACTCGCCGTTCGGCTGCTTT
 T  F  D  V  D  R  G  Q  G  E  D  M  V  S  N  S  S  G  P  I  V  A  N  G  V  I  V  A  G  S  T  C  Q  Y  S  P  F  G  C  F

       610       620       630       640       650       660       670       680       690       700       710       720
GTCTCGGGCCACGACTCGGCCACCGGTGAAGAGCTGTGGCGCAACTACTTCATCCCGCGCGCTGGCGAAGAGGGTGATGAGACTTGGGGCAACGATTACGAAGCCCGTTGGATGACCGGT
 V  S  G  H  D  S  A  T  G  E  E  L  W  R  N  Y  F  I  P  R  A  G  E  E  G  D  E  T  W  G  N  D  Y  E  A  R  W  M  T  G

       730       740       750       760       770       780       790       800       810       820       830       840
GCCTGGGGCCAGATCACCTATGACCCCGTCACCAACCTTGTCCACTACGGCTCGACCGCTGTGGGTCCGGCGTCGGAAACCCAACGCGGCACCCCGGGCGGCACGCTGTACGGCACGAAC
 A  W  G  Q  I  T  Y  D  P  V  T  N  L  V  H  Y  G  S  T  A  V  G  P  A  S  E  T  Q  R  G  T  P  G  G  T  L  Y  G  T  N
         4 = [illegible] check SM
       850       860       870       880       890       900       910       920       930       940       950       960
ACCCGTTTCGCCGTGCGTCCTGACACGGGCGAGATTGTCTGGCGTCACCAGACCCTGCCCCGCGACAACTGGGACCAGGAATGCACGTTCGAGATGATGGTCACCAATGTGGATGTCCAA
 T  R  F  A  V  R  P  D  T  G  E  I  V  W  R  H  Q  T  L  P  R  D  N  W  D  Q  E  C  T  F  E  M  M  V  T  N  V  D  V  Q

       970       980       990      1000      1010      1020      1030      1040      1050      1060      1070      1080
CCCTCGACCGAGATGGAAGGTCTGCAGTCGATCAACCCGAACGCCGCAACTGGCGAGCGTCGCGTGCTGACCGGCGTTCCGTGCAAAACCGGCACCATGTGGCAGTTCGACGCCGAAACC
 P  S  T  E  M  E  G  L  Q  S  I  N  P  N  A  A  T  G  E  R  R  V  L  T  G  V  P  C  K  T  G  T  M  W  Q  F  D  A  E  T

      1090      1100      1110      1120      1130      1140      1150      1160      1170      1180      1190      1200
GGCGAATTCCTGTGGGCCCGTGATACCAACTACCAGAACATGATCGAATCCATCGACGAAAACGGCATCGTGACCGTGAACGAAGATGCGATCCTGAAGGAACTGGATGTTGAATATGAC
 G  E  F  L  W  A  R  D  T  N  Y  Q  N  M  I  E  S  I  D  E  N  G  I  V  T  V  N  E  D  A  I  L  K  E  L  D  V  E  Y  D

      1210      1220      1230      1240      1250      1260      1270      1280      1290      1300      1310      1320
GTCTGCCCGACCTTCTTGGGCGGCCGCGACTGGCCGTCGGCCGCACTGAACCCCGACAGCGGCATCTACTTCATCCCGCTGAACAACGTCTGCTATGACATGATGGCCGTCGATCAGGAA
 V  C  P  T  F  L  G  G  R  D  W  P  S  A  A  L  N  P  D  S  G  I  Y  F  I  P  L  N  N  V  C  Y  D  M  M  A  V  D  Q  E

      1330      1340      1350      1360      1370      1380      1390      1400      1410      1420      1430      1440
TTCACCTCGATGGACGTCTATAACACCAGCAACGTGACCAAGCTGCCGCCCGGCAAGGATATGATCGGTCGTATTGACGCGATCGACATCAGCACGGGTCGTACGCTGTGGTCGGTCGAA
 F  T  S  M  D  V  Y  N  T  S  N  V  T  K  L  P  P  G  K  D  M  I  G  R  I  D  A  I  D  I  S  T  G  R  T  L  W  S  V  E

      1450      1460      1470      1480      1490      1500      1510      1520      1530      1540      1550      1560
CGTGCTGCGGCGAACTATTCGCCCGTCTTGTCGACCGGCGGCGGCGTTCTGTTCAACGGTGGTACGGATCGTTACTTCCGCGCCCTCAGCCAAGAAACCGGCGAGACCCTGTGGCAGACC
 R  A  A  A  N  Y  S  P  V  L  S  T  G  G  G  V  L  F  N  G  G  T  D  R  Y  F  R  A  L  S  Q  E  T  G  E  T  L  W  Q  T

      1570      1580      1590      1600      1610      1620      1630      1640      1650      1660      1670      1680
CGCCTTGCAACCGTCGCGTCGGGCCAGGCCATCTCTTACGAGGTTGACGGCATGCAATATGTCGCCATCGCAGGTGGTGGTGTCAGCTATGGCTCGGGCCTGAACTCGGCACTGGCTGGC
 R  L  A  T  V  A  S  G  Q  A  I  S  Y  E  V  D  G  M  Q  Y  V  A  I  A  G  G  G  V  S  Y  G  S  G  L  N  S  A  L  A  G

      1690      1700      1710      1720      1730      1740
GAGCGAGTCGACTCGACCGCCATCGGTAACGCCGTCTACGTCTTCGCCCTGCCGCAATAA
 E  R  V  D  S  T  A  I  G  N  A  V  Y  V  F  A  L  P  Q  *
```

44/70

A''-1

A''

4/5/89 Sn MG→AM

GENIAS - Amino Acid Translation

DNA Sequence Name (1): ENZA''   (1-2284)
Comment :

> Genetic Code [Universal]

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                                                      TGCCATAGCCCATCGCGCCCAGCGACAGCGCCGATACGCGCAGCCCTTGGCCAAGTTCACGGGTGA
TCATGGTGCAACTCCCCTCTCTGTGCCGTTTGCCGTTAGGATTAAAGGCATCTGGACGCAGGATGACAATATCATCTGGCGGCTAGGGCCTATGCGGGATCAGGATCAATCGCCATGCAA
GTCATGCAATCATTTTAGGCACTTAAAACTTGCGAATCGCGACAATTTGCCCCAGCGTGCTTTTGTCTCATGCGTATCTTCTCGGAGGAGAGGGATGCGTTTATGCGTTGGAGGACAGAG

        10        20        30        40        50        60        70        80        90       100       110       120
ATGAAACTGACGACCCTGCTGCAAAGCAGCGCCGCCCTGCTTGTGCTTGGCACCATTCCCGCCCTTGCCCAAACCGCCATCACCGATGAAATGCTGGCGAACCCGCCCGCTGGTGAATGG
 M  K  L  T  T  L  L  Q  S  S  A  A  L  L  V  L  G  T  I  P  A  L  A  Q  T  A  I  T  D  E  M  L  A  N  P  P  A  G  E  W

       130       140       150       160       170       180       190       200       210       220       230       240
ATCAACTACGGTCAGAACCAAGAGAACTACCGCCACTCGCCCCTGACGCAGATTACCGCAGACAACGTCGGCCAACTGCAACTGGTCTGGGCGCGCGGTATGGAAGCGGGCAAGATCCAA
 I  N  Y  G  Q  N  Q  E  N  Y  R  H  S  P  L  T  Q  I  T  A  D  N  V  G  Q  L  Q  L  V  W  A  R  G  M  E  A  G  K  I  Q

       250       260       270       280       290       300       310       320       330       340       350       360
GTGACCCCGCTTGTCCATGACGGCGTCATGTATCTGGCAAACCCCGGTGACGTGATCCAGGCCATCGACGCCGCGACCGGCGATCTGATCTGGGAACACCGCCGCCAACTGCCGAACATC
 V  T  P  L  V  H  D  G  V  M  Y  L  A  N  P  G  D  V  I  Q  A  I  D  A  A  T  G  D  L  I  W  E  H  R  R  Q  L  P  N  I

       370       380       390       400       410       420       430       440       450       460       470       480
GCCACGCTGAACAGCTTTGGTGAGCCGACCCGCGGCATGGCCCTCTATGGCACCAACGTCTATTTCGTCTCGTGGGACAACCACTTGGTCGCGCTGGACACCTCGACCGGCCAAGTCGTA
 A  T  L  N  S  F  G  E  P  T  R  G  M  A  L  Y  G  T  N  V  Y  F  V  S  W  D  N  H  L  V  A  L  D  T  S  T  G  Q  V  V

       490       500       510       520       530       540       550       560       570       580       590       600
TTCGACGTCGATCGCGGTCAAGGCACGGATATGGTCTCGAACTCGTCCGGCCCGATTGTCGCCAATGGCGTCATCGTTGCGGGCTCGACCTGTCAGTATTCGCCGTTCGGCTGTTTCGTT
 F  D  V  D  R  G  Q  G  T  D  M  V  S  N  S  S  G  P  I  V  A  N  G  V  I  V  A  G  S  T  C  Q  Y  S  P  F  G  C  F  V

       610       620       630       640       650       660       670       680       690       700       710       720
TCGGGCCACGACTCGGCCACCGGTGAAGAGCTGTGGCGCAACACCTTTATCCCGCGCGCCGGCGAAGAGGGTGATGAGACCTGGGGCAATGATTACGAGGCCCGCTGGATGACCGGCGTT
 S  G  H  D  S  A  T  G  E  E  L  W  R  N (T) F  I  P  R  A  G  E  E  G  D  E  T  W  G  N  D  Y  E  A  R  W  M  T  G  V

       730       740       750       760       770       780       790       800       810       820       830       840
TGGGGCCAGATCACCTATGACCCCGTTGGCGGCCTTGTCCACTACGGCACCTCAGCAGTTGGCCCTGCGGCCGAGATTCAGCGCGGCACCGTTGGCGGCTCGATGTATGGCACCAACACC
 W  G  Q  I  T  Y  D  P  V  G  G  L  V  H  Y  G  T  S  A  V  G  P  A  A  E  I  Q  R  G  T  V  G  G  S  M  Y  G  T  N  T

       850       860       870       880       890       900       910       920       930       940       950       960
CGCTTTGCTGTCCGCCCCGAGACCGGCGAGATCGTCTGGCGTCACCAAACTCTGCCCCGCGACAACTGGGACCAAGAGTGTACGTTCGAGATGATGGTCGTCAACGTCGACGTCCAGCCC
 R  F  A  V  R  P  E  T  G  E  I  V  W  R  H  Q  T  L  P  R  D  N  W  D  Q  E  C  T  F  E  M  M  V  V  N  V  D  V  Q  P

       970       980       990      1000      1010      1020      1030      1040      1050      1060      1070      1080
TCGGCTGAGATGGAAGGCCTGCACGCCATCAACCCCGATGCCGCCACGGGCGAGCGTCGCGTTGTGACCGGCGTTCCGTGCAAGAACGGCACCATGTGGCAGTTCGACGCCGAAACCGGC
 S  A  E  M  E  G  L  H  A  I  N  P  D  A  A  T  G  E  R  R  V  V  T  G  V  P  C  K  N  G  T  M  W  Q  F  D  A  E  T  G

      1090      1100      1110      1120      1130      1140      1150      1160      1170      1180      1190      1200
GAATTCCTGTGGGCGCGCGACACCAGCTATCAGAACCTGATCGAAAGCGTCGATCCCGATGGTCTGGTGCATGTGAACGAAGATCTGGTCGTGACCGAGCTGGAAGTGGCCTATGAAATC
 E  F  L  W  A  R  D  T  S  Y  Q  N  L  I  E  S  V  D  P  D  G  L  V  H  V  N  E  D  L  V  V  T  E  L  E  V  A  Y  E  I

      1210      1220      1230      1240      1250      1260      1270      1280      1290      1300      1310      1320
TGCCCGACCTTCCTGGGTGGCCGCGACTGGCCGTCGGCTGCGCTGAACCCCGATACTGGCATCTATTTCATCCCGCTGAACAACGCCTGTAGCGGTATGACGGCTGTCGACCAAGAGTTC
 C  P  T  F  L  G  G  R  D  W  P  S  A  A  L  N  P  D  T  G  I  Y  F  I  P  L  N  N  A  C  S  G  M  T  A  V  D  Q  E  F

      1330      1340      1350      1360      1370      1380      1390      1400      1410      1420      1430      1440
```
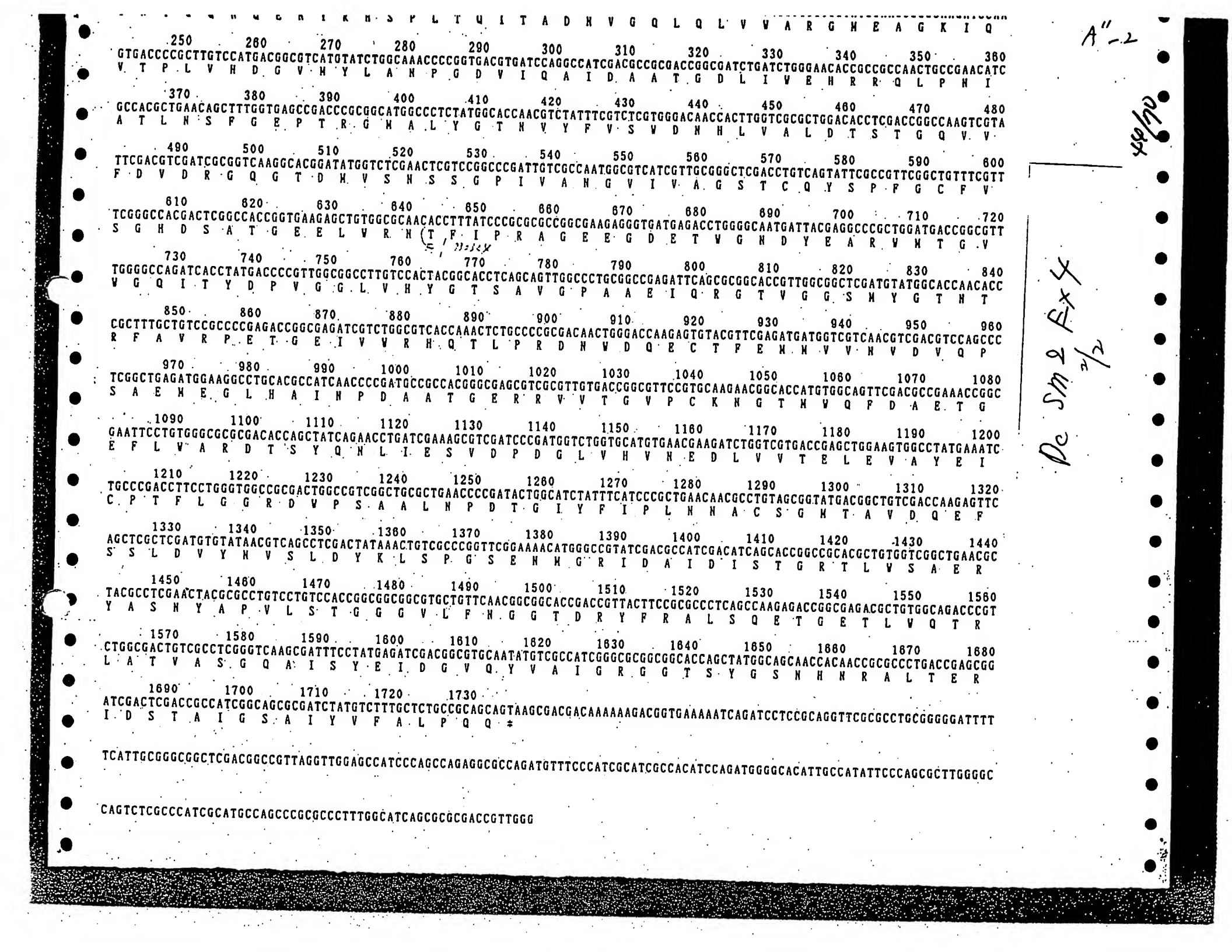

Dc Sm2 Ex4 1/2

43/70


A"-2
Dc Sm 2 Fx4
1/2

D-SM2 Ex 5

Attachment (B)

Sequences of the amplified products.

39F903 (697-1000)/A697f.Seq

TTNCGTGCCT GGGGCCAGAT CACCTATGAC CCCGTCACCA ACCTTGTCCA
CTACGGCTCG ACCGCTGTGG GTCCGGCGTC GGAAACCCAA CGCGGCACCC
CGGGCGGCAC GCTGTACGGC ACGAACACCC GTTTCGCCGT GCGTCCTGAC
ACGGGCGAGA TTGTCTGGCG TCACCAGACC CTGCCCCGCG ACAACTGGGA
CCAGGAATGC ACGTTCGAGA TGATGGTCAC CAATGTGGAT GTCCAACCCT
CGACCGAGAT GGAAGGTCTG CAGTCGATCA ANCGAAANNN NNNNNNNNNN
NNNNN

41F903 (697-1000)/A1000r.Seq

TTCCTCTTGG TCGAGGGTTG GACATCCACA TTGGTGACCA TCATCTCGAA
CGTGCATTCC TGGTCCCAGT TGTCGCGGGG CAGGGTCTGG TGACGCCAGA
CAATCTCGCC CGTGTCAGGA CGCACGGCGA AACGGGTGTT CGTGCCGTAC
AGCGTGCCGC CCGGGGTGCC GCGTTGGGTT TCCGACGCCG GACCCACAGC
GGTCGAGCCG TAGTGGACAA GGTTGGTGAC GGGGTCATAG GTGATCTGGC
CCCAGGCACC GGTCATCCAA CGGGCTTTGT AANNNNNNNN NNNNNNNNNN
N

43F903 (479-780)/A479f.Seq

AAAGCACTTT ATGGNCTCGA ACTCTCCGGC CCGATTGTCG CCAATGGCGT
CATCGTTGCG GGCTCGACCT GTCAGTATTC GCCGTTCGGC TGTTTCGTTT
CGGGCCACGA CTCGGCCACC GGTGAAGAGC TGTGGCGCAA CACCTTTATC
CCGCGCGCCG GCGAAGAGGG TGATGAGACC TGGGGCAATG ATTACGAGGC
CCGCTGGATG ACCGGCGTTT GGGGCCAGAT CACCTATGAC CCCGTTGGCG
GCCTTGTCCA CTACGGCACC TCAAGAGTTA ANANNNNNNN NNNNNNNNN

45F903 (479-780)/A780r.Seq

GACAAGGCTN NCACGGNGTC ATAGGTGATN TGGCCCCAAA CGCCGGTCAT
CCAGCGGGCC TCGTAATCAT TGCCCCAGGT CTCATCACCC TCTTCGCCGG
CGCGCGGGAT AAAGGTGTTG CGCCACAGCT CTTCACCGGT GGCCGAGTCG
TGGCCCGAAA CGAAACAGCC GAACGGCGAA TACTGACAGG TCGAGCCCGC
AACGATGACG CCATTGGCGA CAATCGGGCC GGACGAGTTC GAGACCATAT
CCGTGCCTTG ACCGCGATCG ACGTCCATAA ANNNNNNNNN NNNNNNNNNN

48/70